```
=> d que stat l19
L1             3 SEA FILE=REGISTRY ABB=ON  (12-HETE OR 11,12-EET)/CN
L2             1 SEA FILE=REGISTRY ABB=ON  "EPOXYEICOSATRIENOIC ACID"/CN
L3             4 SEA FILE=REGISTRY ABB=ON  L1 OR L2
L4             1 SEA FILE=REGISTRY ABB=ON  "12-HYDROPEROXY-5,8,10,14-EICOSATETRA
                  ENOIC ACID"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  "13-HYDROPEROXY-9Z,11E,15Z-OCTADECATR
                  IENOIC ACID"/CN
L6             1 SEA FILE=REGISTRY ABB=ON  "13-HYDROPEROXY-9-CIS-11-TRANS-OCTADE
                  CADIENOIC ACID"/CN
L7             3 SEA FILE=REGISTRY ABB=ON  L4 OR L5 OR L6
L9          1467 SEA FILE=HCAPLUS ABB=ON  (L3 OR 12-HETE OR 11,12-EET) AND
                  (?PREPARE? OR ?PRODUC? OR ?MANUFAC? OR ?SYNTHESIZ?)
L10          857 SEA FILE=HCAPLUS ABB=ON  (?CHONDRUS? OR RED?(W)?ALGAE?) AND
                  (?PEPTID? OR ?LIPID? OR ?SACCHARID? OR ?GREEN?(W)?ALGAE? OR
                  ?ACROCHAETE?(W)?OPERCULATA? OR L7 OR 12-HPETE OR 13-HPOTE OR
                  13-HPODE)
L11            2 SEA FILE=HCAPLUS ABB=ON  L9 AND L10
L12           33 SEA FILE=HCAPLUS ABB=ON  L9 AND (?THALLUS? OR ?HORMONE?)
L13           34 SEA FILE=HCAPLUS ABB=ON  L11 OR L12
L19           30 SEA FILE=HCAPLUS ABB=ON  L13 AND (PRD<20020802 OR PD<20020802)

=> d ibib abs l19 1-30

L19  ANSWER 1 OF 30  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2001:594620  HCAPLUS
DOCUMENT NUMBER:          136:272910
TITLE:                    Effects of angiotensin converting enzyme inhibitors on
                          renal p450 metabolism of arachidonic acid
AUTHOR(S):                Ito, Osamu; Roman, Richard J.; Omata, Ken; Takeuchi,
                          Kazuhisa; Ito, Sadayoshi
CORPORATE SOURCE:         Department of Nephrology, Endocrinology and
                          Hypertension, Tohoku University Graduate School of
                          Medicine, Sendai, Japan
SOURCE:                   Therapeutic Research (2001), 22(6),
                          1251-1254
                          CODEN: THREEL; ISSN: 0289-8020
PUBLISHER:                Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE:            Journal
LANGUAGE:                 Japanese
AB   The present study examined the effects of angiotensin converting enzyme
     (ACE) inhibitors and an angiotensin II type 1 (AT1) receptor antagonist on
     the metabolism of arachidonic acid (AA) in the kidney. Male Sprague-Dawley
     rats were treated with vehicle, captopril, enalapril, or candesartan for
     one week. The production of 20-hydroxyeicosatetraenoic acid
     (20-HETE) and epoxyeicosatrienoic acids (EETs) by renal microsomes
     increased in rats treated with captopril and enalapril. In contrast,
     blockade of the AT1 receptors with candesartan had no effect on the
     production of these metabolites. Captopril and enalapril increased
     the expression of P 450 4A protein and P 450 reductase protein in renal
     microsomes. The effects of captopril on the renal metabolism of AA were
     blocked by either HOE-140, a bradykinin type 2 receptor antagonist or
     L-NAME, a nitric oxide (NO) synthase inhibitor. These results suggest
     that ACE inhibitors increase the expression of P 450 4A and P 450
     reductase proteins in the kidney and enhance the formation of 20-HETE and
     EETs secondary to increases in intrarenal levels of kinin and NO.

L19  ANSWER 2 OF 30  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2001:309506  HCAPLUS
DOCUMENT NUMBER:          135:102278
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TITLE: Effects of converting enzyme inhibitors on renal P-450 metabolism of arachidonic acid
AUTHOR(S): Ito, Osamu; Omata, Ken; Ito, Sadayoshi; Hoagland, Kimberly M.; Roman, Richard J.
CORPORATE SOURCE: Department of Nephrology, Endocrinology, Tohoku University Graduate School of Medicine, Sendai, 980-8574, Japan
SOURCE: American Journal of Physiology (**2001**), 280(3, Pt. 2), R822-R830
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of blockade of the renin-angiotensin system on the renal metabolism of arachidonic acid (AA) were examined Male Sprague-Dawley rats were treated with vehicle, captopril (25 mg·kg-1·day-1), enalapril (10 mg·kg-1·day-1), or candesartan (1 mg·kg-1·day-1) for 1 wk. The **production** of 20-hydroxyeicosatetraenoic acid (20-HETE) and epoxyeicosatrienoic acids (EETs) by renal cortical microsomes increased in rats treated with captopril by 59 and 24% and by 90 and 58% in rats treated with enalapril. Captopril and enalapril increased 20-HETE **production** in the outer medulla by 100 and 143%, resp. In contrast, blockade of ANG II type 1 receptors with candesartan had no effect on the renal metabolism of AA. Captopril and enalapril increased cytochrome P 450 (CYP450) reductase protein levels in the renal cortex and outer medulla and the expression of CYP450 4A protein in the outer medulla. The effects of captopril on the renal metabolism of AA were prevented by the bradykinin-receptor antagonist, HOE-140, or the nitric oxide (NO) synthase inhibitor, NG-nitro-L-arginine Me ester. These results suggest that angiotensin-converting enzyme inhibitors may increase the formation of 20-HETE and EETs secondary to increases in the intrarenal levels of kinins and NO.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:780254 HCAPLUS
DOCUMENT NUMBER: 134:27748
TITLE: Renal and cardiovascular actions of 20-hydroxyeicosatetraenoic acid and epoxyeicosatrienoic acids
AUTHOR(S): Roman, Richard J.; Maier, Kristopher G.; Sun, Cheng-Wen; Harder, David R.; Alonso-Galicia, Magdalena
CORPORATE SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: Clinical and Experimental Pharmacology and Physiology (**2000**), 27(11), 855-865
CODEN: CEXPB9; ISSN: 0305-1870
PUBLISHER: Blackwell Science Asia Pty Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 113 refs. Arachidonic acid (AA) is metabolized by cytochrome P 450 (CYP)-dependent pathways to epoxyeicosatrienoic acids (EET) and 20-hydroxyeicosatetraenoic acid (20-HETE) in the kidney and the peripheral vasculature. The present short review summarizes the renal and cardiovascular actions of these important mediators. Epoxyeicosatrienoic acids are vasodilators **produced** by the endothelium that hyperpolarize vascular smooth muscle (VSM) cells by opening Ca2+-activated K+ (KCa) channels. 20-Hydroxyeicosatetraenoic acid is a vasoconstrictor

that inhibits the opening of KCa channels in VSM cells. Cytochrome P 450 4A inhibitors block the myogenic response of small arterioles to elevations in transmural pressure and autoregulation of renal and cerebral blood flow in vivo. Cytochrome P 450 4A blockers also attenuate the vasoconstrictor response to elevations in tissue Po2, suggesting that this system may serve as a vascular oxygen sensor. Nitric oxide and carbon monoxide inhibit the formation of 20-HETE and a fall in 20-HETE levels contributes to the activation of KCa channels in VSM cells and the vasodilator response to these gaseous mediators. 20-Hydroxyeicosatetraenoic acid also mediates the inhibitory actions of peptide **hormones** on sodium transport in the kidney and the mitogenic effects of growth factors in VSM and mesangial cells. A deficiency in the renal **production** of 20-HETE is associated with the development of hypertension in Dahl salt-sensitive rats. In summary, the available evidence indicates that CYP metabolites of AA play a central role in the regulation of renal, pulmonary and vascular function and that abnormalities in this system may contribute to the pathogenesis of cardiovascular diseases.

REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:502750 HCAPLUS
DOCUMENT NUMBER: 125:191516
TITLE: Regulation of Na-K-ATPase activity in the proximal tubule: role of the protein kinase C pathway and of eicosanoids
AUTHOR(S): Ominato, M.; Satoh, T.; Katz, A. I.
CORPORATE SOURCE: Department Medicine, University Chicago Pritzker School Medicine, Chicago, IL, 60637, USA
SOURCE: Journal of Membrane Biology (**1996**), 152(3), 235-243
CODEN: JMBBBO; ISSN: 0022-2631
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate further the signal transduction mechanisms involved in the short-term modulation of Na-K-ATPase activity in the mammalian kidney, we examined the role of phospholipase C-protein kinase C (PLC-PKC) pathway and of various eicosanoids in this process, using microdissected rat proximal convoluted tubules. Dopamine (DA) and parathyroid **hormone** (either synthetic PTH1-34 or PTH3-34) inhibited Na-K-ATPase activity in dose-dependent manner; this effect was **reproduced** by PKC530-558 fragment and blocked by the specific PKC inhibitor calphostin C, as well as by the PLC inhibitors neomycin and U-73122. Pump inhibition by DA, PTH, or arachidonic acid, and by PKC activators phorbol dibutyrate (PDBu) or dioctanoyl glycerol (DiC8) was abolished by ethoxyresorufin, an inhibitor of the cytochrome P 450-dependent monooxygenase pathway, but was unaffected by indomethacin or nordihydroguaiaretic acid, inhibitors of the cyclooxygenase and lipoxygenase pathways of the arachidonic acid cascade, resp. Furthermore, each of the three monooxygenase **products** tested (20-HETE, 12(R)-HETE, or 11,12-DHT) caused a dose-dependent inhibition of the pump. The effect of DA, PTH, PDBu or DiC8, as well as that of 20-HETE was not altered when sodium entry was blocked with the amiloride analog ethylisopropyl amiloride or increased with nystatin. We conclude that short-term regulation of proximal tubule Na-K-ATPase activity by dopamine and parathyroid **hormone** occurs via the PLC-PKC signal transduction pathway and is mediated by cytochrome P 450-dependent monooxygenase **products** of arachidonic acid metabolism,

which may interact with the pump rather than alter sodium access to it.

L19 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:845775 HCAPLUS
DOCUMENT NUMBER: 123:251997
TITLE: Roles of arachidonic acid, lipoxygenases and phosphatases in calcium-dependent modulation of M-current in bullfrog sympathetic neurons
AUTHOR(S): Yu, Shan Ping
CORPORATE SOURCE: Howard Hughes Medical Institute, State University of New York at Stony Brook, Stony Brook, NY, 11794, USA
SOURCE: Journal of Physiology (Cambridge, United Kingdom) (**1995**), 487(3), 797-811
CODEN: JPHYA7; ISSN: 0022-3751
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB M-current (IM) is regulated by intracellular free Ca2+ ([Ca2+]i). Suppression and overrecovery of IM induced by muscarine and luteinizing-**hormone** releasing-**hormone** (LHRH) are also regulated by [Ca2+]i. The role of the arachidonic acid (AA) pathway in the Ca2+-dependent modulation of IM was investigated using whole-cell voltage clamp and intracellular perfusion in dissociated bullfrog sympathetic B neurons. Quinacrine (10-20 μM) and 4-bromophenacyl bromide (4-BPB; 4-10 μM), the inhibitors of phospholipase A2, blocked the enhancement of IM evoked by raising [Ca2+]i. AA (6-120 μM) increased IM by about 50% of the control current in a Ca2+-dependent manner. Enhancements of IM by Ca2+ and AA were blocked by the lipoxygenase (LO) inhibitors nordihydroguaiaretic acid (NDGA; 1-5 μM) and 5,8,11-eicosatrienoic acid (ETI; 10 μM). The cyclooxygenase inhibitor indomethacin (10 μM) had no effect. Enhancement of IM by Ca2+ was abolished by the selective 12-LO inhibitors baicalein (1-2 μM) and 15(S)-hydroxy-5-cis-11-cis-13-trans-eicosatetraenoic acid (15-HETE; 6.5 μM). A 12-LO **product**, 2(S)-hydroxy-5-cis-8-cis-10-trans-14-cis-eicosatetraenoic acid (**12-HETE**; 13-20 μM), increased IM without Ca2+ requirement. Enhancement of IM by Ca2+ was not affected by the selective 5-LO inhibitors AA-861 (10 μM), 5,6-dehydroarachidonic acid (5,6-DAA, 10 μM) and L-651,896 (10 μM). The 5-LO metabolites leukotriene C4 (1·5-8 μM) and leukotriene B4 (1·5-5 μM) showed no obvious effect on IM. NDGA alone inhibited IM with an IC50 of 0.73 μM at 120 nM Ca2+. NDGA did not affect suppression of IM by muscarine or LHRH, however, overrecovery of IM upon removing these agonists was totally eliminated by 1 μM NDGA. Inhibitors of phosphatases, calyculin A (0.1 μM) and okadaic acid (1 μM), completely abolished overrecovery of IM. Calyculin A also blocked the Ca2+-induced IM enhancement. It is suggested that Ca2+ enhances IM by stimulating the AA metabolic pathway. Dephosphorylation probably upregulates IM. Overrecovery of IM is probably a result of stimulation of the LO pathway and phosphatases by increased [Ca2+]i.

L19 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:571055 HCAPLUS
DOCUMENT NUMBER: 121:171055
TITLE: Effects of lipoxygenase **products** of arachidonate metabolism on parathyroid **hormone** secretion
AUTHOR(S): Bourdeau, Agnes; Moutahir, Mohammed; Souberbielle, Jean-Claude; Bonnet, Philippe; Herviaux, Patricia; Sachs, Charles; Lieberherr, Michele
CORPORATE SOURCE: Hop. Necker-Enfants Malades, Univ. Paris V, Paris, Fr.

SOURCE: Endocrinology (**1994**), 135(3), 1109-12
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English
AB High extracellular Ca2+ (Ca2+ec) stimulates the formation of inositol phosphates and diacylglycerol and activates phospholipase A2 in porcine parathyroid cells. Ca2+ec action is also coupled to the formation of arachidonic acid, the precursor of both the cyclooxygenase and lipoxygenase (LO) pathways. We previously reported that LO pathway **products** might act as second messengers and play a part in regulating PTH secretion by Ca2+ec. We have now investigated the effects of hydroxyeicosatetraenoic acids (HETEs) on PTH secretion. Collagenase-dispersed porcine parathyroid cells were incubated in low [Ca2+] (0.5 mM, maximal stimulation) with or without HETEs for three 15-min periods. 12- And 15-HETEs inhibited PTH secretion in a dose-dependent manner from 10-12 to 10-9 M. Maximal inhibition was with 10-9 M. Since 12- and 15-HETEs are the metabolic reduction **products** of 12- and 15-HPETEs, we also examined the effect of those precursors on PTH release. 12- And 15-hydroperoxyeicosatetraenoic acids (HPETEs) were more potent inhibitors of PTH secretion. The threshold concns. of both HPETEs that inhibited PTH release were lower than those for HETEs: 10-9 M suppressed PTH secretion. This effect is comparable to that of high [Ca2+] (2 mM). This provides new evidence that **products** of 12-LO and 15-LO pathways are potent inhibitors of PTH secretion.

L19 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:140038 HCAPLUS
DOCUMENT NUMBER: 118:140038
TITLE: Structural and functional evidence for activation of a chick retinoid X receptor by eicosanoids
AUTHOR(S): Eager, Nicholas S. C.; Brickell, Paul M.; Snell, Christopher; Wood, John N.
CORPORATE SOURCE: Middlesex Sch. Med., Univ. Coll., London, UK
SOURCE: Proceedings of the Royal Society of London, Series B: Biological Sciences (**1992**), 250(1327), 63-9
CODEN: PRLBA4; ISSN: 0080-4649
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The retinoid X receptors (RXR-α, RXR-β, and RXR-γ) are members of the steroid-thyroid **hormone** receptor superfamily of ligand-dependent transcription factors. They appear to function as auxiliary proteins that regulate high-affinity DNA binding and enhance transcriptional activity through heterodimer formation with other members of the superfamily. The RXR-α, RXR-β and RXR-γ proteins bind and are activated by the naturally occurring retinoid, 9-cis-retinoic acid. Structural similarities are apparent between retinoic acid and various eicosanoids, raising the possibility that eicosanoids may also activate retinoid receptors in vivo. Evidence is presented that lipoxygenase metabolites of arachidonic acid at submicromolar concns. are capable of activating RXR-γ activity in transient transfection assays. In addition, mol. modeling predicts conformational similarities between some lipoxygenase **products** and retinoic acid. Consistent with this, hydroxyeicosatetraenoic acids are known to mimic some actions of retinoids in cell-based assays. These observations raise the possibility that eicosanoids, already known to act both as local **hormones** and as intracellular second messengers, may also have a direct role in transcriptional activation via nuclear receptors.

L19 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:52817 HCAPLUS

DOCUMENT NUMBER: 118:52817
TITLE: Selective expression of an arachidonate 12-lipoxygenase by pancreatic islet β-cells
AUTHOR(S): Shannon, Vickie R.; Ramanadham, Sasanka; Turk, John; Holtzman, Michael J.
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SOURCE: American Journal of Physiology (**1992**), 263(5, Pt. 1), E828-E836
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The immunohistochem. distribution of arachidonate lipoxygenases in rat pancreas was characterized with specific polyclonal anti-5-lipoxygenase and anti-12-lipoxygenase antibodies. Immunohistochem. anal. of formaldehyde-fixed paraffin-embedded rat pancreas using anti-12-lipoxygenase antibody and biotin-avidin-peroxidase detection demonstrated specific staining of islets and no staining of pancreatic exocrine tissue. Less intense staining of pancreatic vascular myocytes and endothelial cells was also observed Immunoblotting of isolated pancreatic islet exts. with the anti-12-lipoxygenase antibody demonstrated immunoperoxidase staining of a single protein band which comigrated with purified 12-lipoxygenase antibody (relative mol. weight = 72,000) on sodium dodecyl sulfate-polyacrylamide gel electrophoresis anal. Dispersed cells **prepared** from isolated islets and then subjected to fluorescence-activated cell sorting and immunostaining exhibited 12-lipoxygenase antigen in β-cell populations but not in non-β-cell (predominantly-α-cell) populations. Assays of enzymic activity confirmed that the 12-hydroxyeicosatetraenoic acid Me ester occurred only with purified β-cells and not with islet non-β-cells. No evidence of 5-lipoxygenase antigen or enzymic activity was found in purified β-cells or in islet non-β-cells. Thus, rat pancreatic islet β-cells contain an arachidonate 12-lipoxygenase which shares antigenic epitopes with the homologous enzyme contained in tissues from other species. In addition, the selective localization of the 12-lipoxygenase to pancreatic β-cells and its absence in pancreatic acinar cells and in islet non-β-cells support observations suggesting that 12-lipoxygenase **products** may participate in glucose-induced insulin secretion from β-cells.

L19 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:544270 HCAPLUS
DOCUMENT NUMBER: 117:144270
TITLE: 12-Lipoxygenase **products** modulate calcium signals in vascular smooth muscle cells
AUTHOR(S): Saito, Fumio; Hori, Mark T.; Ideguchi, Yasufumi; Berger, Morris; Golub, Michael; Stern, Naftali; Tuck, Michael L.
CORPORATE SOURCE: Div. Endocrinol., Veterans Adm. Med. Cent., Sepulveda, CA, 91343, USA
SOURCE: Hypertension (**1992**), 20(2), 138-43
CODEN: HPRTDN; ISSN: 0194-911X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, the effects of lipoxygenase inhibitors on pressor-induced changes in the cytosolic calcium were examined in cultured rat vascular smooth muscle cells using the fluorescent dye fura-2. Two structurally unrelated lipoxygenase inhibitors, baicalein and 4,8,11-eicosatriynoic acid, attenuated angiotensin II-stimulated increases in cytosolic calcium in both normal and calcium-poor buffer. The addn of 5-, 12-, or 15( S)-hydroxyeicosatetraenoic acid alone to the cells had no

acute effect on intracellular calcium concentration However, the addition of 12(S)-hydroxyeicosatetraenoic acid but not 5- or 15(S)-hydroxyeicosatetraenoic acid restored the initial calcium response to angiotensin II in vascular smooth muscle cells pretreated with both inhibitors; 3,8,11-eicosatriynoic acid also reduced [Arg8]-vasopressin and endothelin-stimulated increases in intracellular calcium. The attenuation of vasopressor-induced calcium transients by agents that inhibit lipoxygenase may explain their observed hypotensive effects in vivo. Moreover, lipoxygenase **products**, in particular 12(S)-hydroxyeicosatetraenoic acid, may act as mediators for the intracellular actions of angiotensin II and possibly other pressor **hormones** in vascular tissue by regulation of intracellular calcium metabolism

L19 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:445028 HCAPLUS
DOCUMENT NUMBER: 117:45028
TITLE: Effects of neurohypophyseal and adenohypophyseal **hormones**, steroids, eicosanoids, and extrafollicular tissue on ovulation in vitro of guppy (Poecilia reticulata) embryos
AUTHOR(S): Venkatesh, B.; Tan, C. H.; Lam, T. J.
CORPORATE SOURCE: Dep. Zool., Natl. Univ. Singapore, Singapore, 0511, Singapore
SOURCE: General and Comparative Endocrinology (**1992**), 87(1), 20-7
CODEN: GCENA5; ISSN: 0016-6480
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the viviparous guppy, oocyte maturation is followed by intrafollicular fertilization and gestation. The fully developed embryos are ovulated at term just prior to parturition. Various agents were tested in vitro for their effects on ovulation of embryos in isolated follicles of the guppy. Arachidonic acid (10 and 100 μM), PGE2, PGF2α, and 6-keto-PGF1α (0.1 μg/mL) induced ovulation, while PGE1, 15-keto-PGF2α, LTB4, 5-, 12-, and 15- HETEs (0.01-0.1 μg/mL), cortisol, 11-deoxycortisol (25 and 250 ng/mL), estradiol, testosterone, 17α,20β-dihydroxy-4-pregnen-3-one, progesterone (5 and 50 ng/mL), isotocin, vasotocin (0.02-2 μg/mL), and guppy pituitary extract (1 and 2 glands per fish) did not. Extrafollicular (EF) ovarian tissue cocultured with isolated follicles induced ovulation, and the medium levels of prostaglandin (PG) E and PGF in such incubations were higher than those in the control. Indomethacin, the cyclooxygenase inhibitor, did not inhibit ovulation induced by arachidonic acid and EF tissue, although it inhibited PGE and PGF **production** NDGA, the lipoxygenase inhibitor, did not inhibit ovulation induced by arachidonic acid or EF tissue. A combination of eicosanoids **synthesized** by follicles and EF tissue may be involved in the induction of ovulation. Dibutyryl cAMP inhibited ovulation induced by PGE2, PGF2α, 6-keto-PGF1α, and EF tissue suggesting that a low level of cAMP may be associated with ovulation in the guppy.

L19 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:424072 HCAPLUS
DOCUMENT NUMBER: 117:24072
TITLE: Renal cytochrome P-450-arachidonic acid metabolism: localization and hormonal regulation in SHR
AUTHOR(S): Omata, Ken; Abraham, Nader G.; Schwartzman, Michal Laniado
CORPORATE SOURCE: Dep. Pharmacol. Med., New York Med. Coll., Valhalla,

NY, 10595, USA
SOURCE: American Journal of Physiology (**1992**), 262(4, Pt. 2), F591-F599
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epoxygenase and ω- and ω-1-hydroxylases are the major cytochrome P 450-arachidonate (P 450-AA) metabolizing enzymes in renal tissues. The authors measured P 450-AA metabolism in single nephron segments and determined the tubular localization of this activity in spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY). Formation of 20-hydroxyeicosatetraenoic acid (20-HETE), the **product** of AA ω-hydroxylase, was specifically localized in the entire proximal tubules (S1, S2, and S3 segments), whereas formation of 19-HETE, the **product** of ω-1-hydroxylase, and epoxyeicosatrienoic acids (EETs), **products** of AA epoxygenase, was demonstrable throughout the tubule. Although distribution patterns were similar in SHR and WKY, formation of 19- and 20-HETE in the proximal tubules was higher in SHR, whereas the formation of EETs was not different between the two strains. In the proximal tubules, angiotensin II (ANG II) stimulated epoxygenase activity (EETs formation), whereas parathyroid **hormone** (PTH) and epidermal growth factor (EGF) had no effect on epoxygenase but stimulated ω-hydroxylase activity (20-HETE formation). Because P 450-AA metabolites have a wide and contrasting spectrum of biol. and renal effects, from vasodilation to vasoconstriction and from inhibition to stimulation of Na+-K+-ATPase, their localization to the specific nephron segments and differential stimulation of their formation by ANG II, PTH, and EGF may contribute not only to renal hemodynamics and blood pressure regulation but also to the regulation of renal sodium and water balance.

L19 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:401292 HCAPLUS
DOCUMENT NUMBER: 117:1292
TITLE: Gonadotropin-releasing **hormone** activates the lipoxygenase pathway in cultured pituitary cells: role in gonadotropin secretion and evidence for a novel autocrine/paracrine loop
AUTHOR(S): Dan-Cohen, Hana; Sofer, Yosef; Schwartzman, Michal L.; Natarajan, Rama D.; Nadler, Jerry L.; Naor, Zvi
CORPORATE SOURCE: Tel Aviv Univ., Tel Aviv, 69978, Israel
SOURCE: Biochemistry (**1992**), 31(24), 5442-8
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation and role of arachidonic acid (AA) and its metabolites during gonadotropin-releasing **hormone** (GnRH)-induced gonadotropin secretion were investigated in primary cultures of rat pituitary cells. Prelabeled cells ([3H]AA) responded to GnRH challenge with increased formation (.apprx.2-fold) of the leukotrienes LTC4, LTD4, and LTE4 as well as 5- and 15-eicosatetraenoic acids (5- and 15-HETE) as identified by HPLC. Formation of leukotrienes and 15-HETE was further verified by specific RIAs. No increase in the formation of **12-HETE** or of the cyclooxygenase **products** PGE and TXA2 by GnRH was noticed. Addition of physiol. concns. of LTC4 enhanced basal LH release, while subphysiol. concns. of LTC4 (10-15-10-12M) inhibited GnRH-induced LH release by .apprx.35%. By using specific lipoxygenase inhibitors L 656,224 and MK 886, inhibition of GnRH-induced LH release by .apprx.40% at concns. known to specifically inhibit the 5-lipoxygenase pathway was found. The peptidoleukotriene receptor antagonist ICI 198, 615 inhibited LTC4- and LTE4-induced LH release and surprisingly also the effect of GnRH

on LH release by 40%. The data strongly suggest a role for AA and its lipoxygenase metabolites in the on/off reactions of GnRH upon LH release. The data also present a novel amplification cycle in which newly formed leukotrienes become first messengers and establish an autocrine/paracrine loop.

L19 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:506963 HCAPLUS
DOCUMENT NUMBER: 115:106963
TITLE: Role of epoxygenase metabolites of arachidonic acid in intracellular signal transduction
AUTHOR(S): Hirai, Aizan; Yoshida, Setsuko; Nishimura, Motonobu; Seki, Koichi; Tamura, Yasushi; Yoshida, Sho
CORPORATE SOURCE: Sch. Med., Chiba Univ., Chiba, 280, Japan
SOURCE: Advances in Prostaglandin, Thromboxane, and Leukotriene Research (**1990**), 21B(Prostaglandins Relat. Compd.), 827-30
CODEN: ATLRD6; ISSN: 0732-8141
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Arachidonate metabolites **produced** by the epoxygenase pathway, probably epoxyeicosatrienoic acids (EETs), are apparently involved in vasopressin-induced glycogenolysis by the liver, probably through Ca-mediated pathways. In bovine adrenal fasciculata cells, EET stimulated Ca mobilization and cortisol formation. Thus, the epoxygenase metabolite of arachidonate, probably EET, may be involved in Ca2+-mediated intracellular signal transduction as a Ca mobilizer.

L19 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:182128 HCAPLUS
DOCUMENT NUMBER: 114:182128
TITLE: Eicosanoids from Rhodophyta: new metabolism in the algae
AUTHOR(S): Gerwick, William H.; Bernart, Matthew W.; Moghaddam, Mehran Fallah; Jiang, Zhi D.; Solem, Michele L.; Nagle, Dale G.
CORPORATE SOURCE: Coll. Pharm., Oregon State Univ., Corvallis, OR, 97331, USA
SOURCE: Hydrobiologia (**1990**), 204-205, 621-8
CODEN: HYDRB8; ISSN: 0018-8158
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Red marine algae are a rich source of eicosanoid-type natural **products.** This is the first isolation of several of these mammalian arachidonic acid metabolites from any marine or terrestrial plant source (**12-HETE**, 12-HEPE, 6(E)-LTB4, hepoxilin B3). A few of these represent truly novel substances never previously isolated from nature [12(R), 13(S)-diHETE]. Inherent in these seaweed natural **product** structures is evidence for a highly evolved lipoxygenase-type metabolism that matches or exceeds the complexity of comparable metabolic routes in mammalian systems. As these compds. are **produced** by algae in relatively large quantities (0.1-5.0% of crude **lipid** exts.), these plants could be important com. resources for these expensive and rare biochems. Apparently, this metabolism is important to physiol. processes in **red algae** that are completely unknown at present. For example, it is possible that they act in an exocrine sense to coordinate **reproductive** events, a hypothesis under current investigation through culture studies.

L19 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:136382 HCAPLUS
DOCUMENT NUMBER: 112:136382
TITLE: Cytochrome P450-dependent arachidonic acid metabolism in human kidney
AUTHOR(S): Schwartzman, Michal L.; Martasek, Pavel; Rios, Amelia R.; Levere, Richard D.; Solangi, Karim; Goodman, Alvin I.; Abraham, Nader G.
CORPORATE SOURCE: Dep. Med. Pharmacol., New York Med. Coll., Valhalla, NY, 10595, USA
SOURCE: Kidney International (**1990**), 37(1), 94-9
CODEN: KDYIA5; ISSN: 0085-2538
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytochrome P 450-dependent arachidonic acid metabolism in human kidney cortex from several postmortem subjects was characterized. By using HPLC and gas chromatog./mass spectrometry, 4 cytochrome P 450-arachidonic acid metabolites were tentatively but not unequivocally identified as epoxyeicosatrienoic acid (EET), dihydroxyeicosatrienoic acid (DHT) and 19- and 20-hydroxyeicosatetraenoic acids, suggesting the involvement of 2 major cytochrome P 450 enzymes, epoxygenase (I) and ω/ω-1 hydroxylases. This pattern of metabolism was similar to that found in rabbit and rat kidneys. The formation of these metabolites was dependent on the presence of NADPH and inhibited by IgG of NADPH-cytochrome P 450 (c) reductase. Immunol. studies of renal I demonstrated that antibodies **prepared** against human-purified hepatic I recognized renal enzyme protein and inhibited the enzyme activity by 92%. In contrast, control Ig did not inhibit renal I. Antibody inhibition of renal I demonstrated a degree of conservation of both enzyme proteins between liver and kidney. Antibodies against lauric acid ω/ω-1 hydroxylases (P 450ω) inhibited the formation of ω/ω-1 hydroxylase **products**, 19- and 20-HETEs. Identical qual. patterns of arachidonic acid metabolites were observed in all cortical microsomes studied. Interindividual variations were observed in the cytochrome P 450-dependent arachidonic acid metabolism, and the activities ranged from 0.031 to 5.027 nmol arachidonic acid converted/mg protein/30 min, which is about a 150-fold difference. However, when the specific activities for total cytochrome P 450-dependent arachidonic acid metabolism were calculated, 2 sep. groups could be distinguished, high and low metabolizers of arachidonic acid. The range of the low metabolizer of arachidonic acid by cytochrome P 450 was 0.15-0.23 pmol arachidonic acid converted/pmol P 450/min, as compared to the range of the high metabolizer which was 1.38-1.93 pmol arachidonic acid converted/pmol P 450/min. The interindividual variation observed with respect to arachidonic acid metabolism was also observed in other cytochrome P 450 monooxygenase systems studied, aryl hydrocarbon hydroxylase and 7-ethoxyresorufin-O-deethylase. Arachidonate metabolites derived by cytochrome P 450 have been shown to possess a wide range of biol. activities; these include stimulation of peptide **hormone** release, inhibition and stimulation of Na+-K+-ATPase, vasoreactivity and mobilization of Ca2+. Apparently, the interindividual variations observed in cytochrome P 450-dependent arachidonic acid metabolism may play a role in the susceptibility of certain individuals to develop clin. disorders such as essential hypertension.

L19 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:92442 HCAPLUS
DOCUMENT NUMBER: 112:92442
TITLE: Leukotrienes, but not hydroxyeicosatetraenoic acids, lower blood pressure in pregnant and postpartum rhesus monkeys
AUTHOR(S): Walsh, Scott W.; Parisi, Valerie M.

CORPORATE SOURCE: Univ. Texas Med. Sch., Houston, TX, 77030, USA
SOURCE: Clinical and Experimental Hypertension, Part B: Hypertension in Pregnancy (**1989**), B8(2), 305-29
CODEN: CEHBDP; ISSN: 0730-0085
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leukotrienes (LTs) and hydroxyeicosatetraenoic acids (HETEs) were injected into the lower vena cava of monkeys to mimic the systemic route of placentally **produced hormones.** Tethered, chronically catheterized pregnant and postpartum rhesus monkeys were used. HETEs had no effect. LTB4, LTC4, or LTD4 (5-20 μg, i.v., bolus) decreased maternal systemic arterial blood pressure (systolic by 9 mmHg, diastolic by 7 mmHg) from 15 to 90 s. after administration. A combination of LTB4, LTC4, LTD4 (2 μg each, i.v.) also lowered blood pressure suggesting their effects might be additive. FPL 55,712 (a cysteine LT receptor blocker, 10 mg, i.v., bolus) increased blood pressure (systolic by 15 mmHg, diastolic by 10 mmHg) demonstrating a role for endogenous LTs to lower blood pressure. Higher doses of the LTs, (10 μg or 20 μg) did not increase the vasodilating effects but did **produce** behavioral changes from .apprx.2 to 4 min after administration (eg. sleepiness and lying down with LTC4 and LTD4; agitation, hyperkinesis, loss of coordination and lying down with LTB4). There were addnl. hypotensive periods associated with the behavioral changes . Thus, LTs might affect neurol. function and lower systemic blood pressure by cerebrally mediated effects. Evidently, LTB4, LTC4, and LTD4 decrease maternal systemic arterial blood pressure, probably by vasodilating systemic arterioles; addnl., LT **production** by the placenta may lower maternal blood pressure during normal pregnancy in primates.

L19 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:592441 HCAPLUS
DOCUMENT NUMBER: 111:192441
TITLE: Platelet-neutrophil-smooth muscle cell interactions: lipoxygenase-derived mono- and dihydroxy acids activate cholesteryl ester hydrolysis by the cyclic AMP dependent protein kinase cascade
AUTHOR(S): Hajjar, David P.; Marcus, Aaron J.; Etingin, Orli R.
CORPORATE SOURCE: Med. Coll., Cornell Univ. Med. Coll., New York, NY, 10021, USA
SOURCE: Biochemistry (**1989**), 28(22), 8885-91
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A biochem. effect of lipoxygenase-derived eicosanoids in the modulation of cholesterol metabolism in bovine arterial smooth muscle cells is reported. **Products** of platelet-neutrophil interactions served as cell signals in vitro to modulate cholesterol metabolism 12-Hydroxyeicosatetrolenoic acid (**12-HETE**) 12,20-DiHETE, and **12-HETE**-1,20-dioic acid activate both lysosomal and cytoplasmic cholesteryl ester (CE) hydrolytic activities, although no effect was observed on CE synthetic acyl-CoA: cholesterol O-acyltransferase activity. The platelet lipoxygenase **product**, **12-HETE**, was the most effective stimulator of CE hydrolysis in the smooth muscle cell, and its conversion to 1,20-DiHETE and the dioic acid derivative by the neutrophils was not necessary for the activation of CE hydrolase. A 2-fold enhancement on CE hydrolysis occurred and was independent of any cross-activation by hydroxy acids on **production** of cyclooxygenase or other lipoxygenase **products.** The activation of cytoplasmic CE hydrolysis had a lesser cofactor dependence

on bile salts in the presence of **12-HETE**, suggesting reduced requirement for surface-active agents in an enzyme-substrate interaction where enzymes are hydrolyzing insol. lipid substrates. **12-HETE** induced an additive effect with several lipolytic **hormones** in the activation of CE catabolism. Dose-dependent, increased enhancement of lysosomal and cytoplasmic CE hydrolase activities by these hydroxy and dihydroxy acids was also cAMP-dependent since (1) were was no stimulatory effect on CE hydrolysis in the presence of an inhibitor of adenylate cyclase, which maintained cAMP at basal levels, and (2) these acids enhanced cAMP levels almost 2-fold in the cell, which paralleled the increased level of hydrolytic activities. Mechanistic data further revealed that the cytoplasmic CE hydrolase was activated by the cAMP-dependent protein kinase in the presence of these eicosanoid agonists. Other expts. showed that incubation of **12-HETE** with endothelial or smooth muscle cells did not result in **production** of 12,20-DiHETE or **12-HETE**-1,20-dioic acid. Therefore, the cytochrome P 450 **12-HETE** ω-hydrolase characteristically present in human neutrophils is absent from these arterial cells. Physiol. and pathophysiol. (especially atherosclerosis) implications of the data are described.

L19 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:588187 HCAPLUS
DOCUMENT NUMBER: 111:188187
TITLE: Arachidonic acid metabolites in the rat and human brain. New findings on the metabolism of prostaglandin D2 and lipoxygenase **products**
AUTHOR(S): Wolfe, L. S.; Pellerin, L.
CORPORATE SOURCE: Montreal Neurol. Inst., McGill Univ., Montreal, QC, H3A 2B4, Can.
SOURCE: Annals of the New York Academy of Sciences (**1989**), 559(Arachidonic Acid Metab. Nerv. Syst.), 74-83
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Large amts. of PGD2 were found in the rat brain, but not in that of humans. This species difference was due to the presence of an NADPH-dependent PGD2 11-ketoreductase in the human brain that converted PGD2 to 6α,11β-PGF2. Hydroxyeiocosatetraenoic acids (HETE) were also formed from arachidonate by rat brain pieces in the presence of the Ca ionophore A 23187, with **12-HETE** being the predominant isomer. The formation of **12-HETE** was stimulated by L-glutamate and by norepinephrine, but not by several other neurotransmitters.

L19 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:491084 HCAPLUS
DOCUMENT NUMBER: 111:91084
TITLE: Synthesis and functions of cyclooxygenase and lipoxygenase **products** in brain: new findings and an appraisal
AUTHOR(S): Wolfe, L. S.; Pellerin, L.; Rostworowski, K.; Pappius, H. M.
CORPORATE SOURCE: Montreal Neurol. Inst., McGill Univ., Montreal, QC, H3A 2B4, Can.
SOURCE: Advances in Prostaglandin, Thromboxane, and Leukotriene Research (**1989**), 19(Taipei Conf.

Prostaglandin Leukotrine Res., 1988), 387-93
CODEN: ATLRD6; ISSN: 0732-8141
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The metabolism and neuromodulatory role of PGD2 and the interactions of arachidonate metabolites and biogenic amines in brain injury are reviewed. In addition, glutamate, norepinephrine (NE), N-methyl-D-aspartate, but not kainate stimulated 12-hydroxyeicosatetraenoic acid (**12-HETE**) formation from arachidonate by rat cerebral cortex. The action of NE was mediated by α-adrenoceptors since isoproterenol had no action. Thus, lipoxygenase **products**, **12-HETE**, or its hydroperoy precursor might be important bioregulators in the central nervous system.

L19 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:454171 HCAPLUS
DOCUMENT NUMBER: 111:54171
TITLE: Discovery of 12-(S)-hydroxy-5,8,10,14-eicosatetraenoic acid [12-(S)-HETE] in the tropical red alga Platysiphonia miniata
AUTHOR(S): Moghaddam, M. F.; Gerwick, W. H.; Ballantine, D. L.
CORPORATE SOURCE: Coll. Pharm., Oregon State Univ., Cornwallis, OR, 97331, USA
SOURCE: Prostaglandins (**1989**), 37(2), 303-8
CODEN: PRGLBA; ISSN: 0090-6980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potent mammalian **immunohormone**, 12-(S)-HETE (I) was isolated for the first time from a plant source, e.g. P. miniata, indicating that lipoxygenase-type **products** are present in red algae. I was isolated as 12-(S)-acetoxyicosatetraenoic acid Me ester.

L19 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:166730 HCAPLUS
DOCUMENT NUMBER: 110:166730
TITLE: Stimulation of progesterone and prostaglandin E2 **production** by lipoxygenase metabolites of arachidonic acid
AUTHOR(S): Wang, Jian; Yuen, Basil Ho; Leung, Peter C. K.
CORPORATE SOURCE: Dep. Obstet./Gynaecol., Univ. British Columbia, Vancouver, BC, V6H 3V5, Can.
SOURCE: FEBS Letters (**1989**), 244(1), 154-8
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of several lipoxygenase metabolites of arachidonic acid in the action of LH-RH on ovarian **hormone production** was investigated. Like LH-RH, treatment of rat granulosa cells with 5-hydroxyeicosatetraenoic acid (5-HETE), 5-hydroperoxyeicosatetraenoic acid (5-HPETE), 12-hydroxyeicosatetraenoic acid (**12-HETE**), 15-hydroxyeicosatetraenoic acid (15-HETE), or 15-hydroxyperoxyeicosatetraenoic acid (15-HPTE) stimulated progesterone (P) and PGE2 **production** **12-HETE** was the most potent and stimulated P and PGE2 equally well. By contrast, 5-HETE stimulated P better than PGE2, whereas 15-HETE was a potent stimulator of PGE2 but not of P. Stimulation of P and PGE2 by LH-RH or 12-O-tetradecanoylphorbol 13-acetate was further augmented by several HETEs and HPETEs. Like protein kinase C, arachidonic acid metabolites appear to mediate the multiple actions of LH-RH in the ovary.

L19 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:567814 HCAPLUS
DOCUMENT NUMBER: 109:167814
TITLE: Regulation of liver metabolism by intercellular communication
AUTHOR(S): Kuiper, Johan; Casteleyn, Eric; Van Berkel, Theo J. C.
CORPORATE SOURCE: Cent. Bio-Pharm. Sci., Univ. Leiden, Leiden, 2300 RA, Neth.
SOURCE: Advances in Enzyme Regulation (**1988**), Volume Date 1987, 27, 193-208, 1 plate
CODEN: AEZRA2; ISSN: 0065-2571
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The regulation of rat liver metabolism by intercellular communication was assessed by studying the effect of conditioned media of Kupffer and liver endothelial cells on protein synthesis, protein phosphorylation, and glycogenolysis in parenchymal cells. Kupffer and endothelial cell-conditioned media enhanced the rate of protein synthesis of parenchymal cells by a factor of 1.7-1.9. The phosphorylation state of only 3 specific parenchymal cell proteins was influenced by the conditioned media. The mol. weight 97,000 band appeared to be phosphorylase and in parallel with an enhancement of the activity of phosphorylase the glucose output by parenchymal cells could be stimulated. The effects of the conditioned media could be mimicked by prostaglandin E1, E2 and D2, whereas the pretreatment of nonparenchymal cells with aspirin abolished the stimulatory effect of these cells on the glucose output by parenchymal cells. Thus, prostaglandins from Kupffer and endothelial cells, mainly PGD2, can influence glucose release from parenchymal cells. The tumor-promoting phorbol ester PMA stimulated glycogenolysis in perfused liver 2-fold. This stimulation was blocked by the presence of aspirin. PMA is inactive on isolated parenchymal cells. Addition of PMA to the perfused liver appears to enhance the output of PGD2 in parallel with the stimulation of the glucose output. Addition of PGD2 itself could also stimulate the glucose output in the perfused liver. Thus, stimulation of glycogenolysis in the liver by PMA is mediated by nonparenchymal cells which **produce** PGD2 in response to PMA, leading subsequently to activation of the phosphorylase system in the parenchymal cells. It seems possible also that the tumor-promoting activity of PMA on liver will be mediated by a primary interaction with nonparenchymal cells. The occurrence of intercellular communication inside the liver in response to activation of nonparenchymal cells adds a new mechanism to the complex regulation of liver metabolism which may be relevant under normal and pathol. conditions.

L19 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:564187 HCAPLUS
DOCUMENT NUMBER: 109:164187
TITLE: A possible role for lipoxygenase and epoxygenase arachidonate metabolites in prolactin release from pituitary cells
AUTHOR(S): Judd, Allan M.; Spangelo, Bryan L.; Ehreth, Jeffrey T.; MacLeod, Robert M.
CORPORATE SOURCE: Sch. Med., Univ. Virginia, Charlottesville, VA, USA
SOURCE: Neuroendocrinology (**1988**), 48(4), 407-16
CODEN: NUNDAJ; ISSN: 0028-3835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of selected leukotrienes and hydroxyeicosatetraenoic acids (HETEs) on prolactin release from primary cultures of female rat anterior pituitary cells were studied. Leukotrienes B4, C4, and D4 had no effect

on basal prolactin release; however, they did enhance prolactin release that was stimulated by 1 or 5 nM TSH-releasing **hormone** (TRH). Leukotriene C4 also enhanced prolactin release that was induced by PMA (a protein kinase C activator), by maitotoxin (a Ca uptake stimulator), and by angiotensin II. 5-HETE, **12-HETE**, and 15-HETE stimulated basal prolactin release at high concns. (≤1 μM), and 5-HETE and **12-HETE** enhanced TRH- and angiotensin II-induced prolactin release at lower (nanomolar) concns. as well. To determine the role of endogenous arachidonate metabolites in prolactin release, pituitary cell cultures were exposed to selected inhibitors of the 5-lipoxygenase enzyme, which metabolizes arachidonate to leukotrienes and 5-HETE, and to those of the epoxygenase enzyme, which metabolizes arachidonate to epoxyeicosatrienoic acids. These inhibitors decreased basal and secretagogue-induced prolactin release. In addnl. expts., it was determined that TRH enhances the liberation from pituitary cells of arachidonate metabolites with HPLC elution profiles similar to those of leukotriene C4 and ω-OH-leukotriene B4 (a metabolite of leukotriene B4) and the HETEs. Therefore, the **production** of leukotrienes, HETEs, and epoxyeicosatrienoic acids may be necessary for the normal release of prolactin.

L19 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:490647 HCAPLUS
DOCUMENT NUMBER: 107:90647
TITLE: Blockade of receptor-mediated cyclic GMP formation by hydroxyeicosatetraenoic acid
AUTHOR(S): McKinney, Michael
CORPORATE SOURCE: Abbott Lab., Abbott Park, IL, 60064, USA
SOURCE: Journal of Neurochemistry (**1987**), 49(2), 331-41
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In N1E-115 murine neuroblastoma cells, 15-hydroxyeicosatetraenoic acid (15-HETE), **12-HETE**, and 5-HETE inhibited the cGMP formation after carbachol-induced muscarinic receptor activation with 50% inhibitory concns. (IC50) of 11, 13, and 10 μM, resp. All 3 of these monoHETEs were also inhibitors of the cGMP responses to receptors stimulated by histamine, thrombin, neurotensin, and bradykinin. 15-HETE inhibited the muscarinic receptor-mediated response in a complex manner (apparent noncompetitive and uncompetitive components; IC50 = 18 and 2 μM, resp.). 15-HETE did not inhibit either the M1 muscarinic receptor-stimulated release of [3H]inositol phosphates from cellular phospholipids or the M2 muscarinic receptor-mediated inhibition of **hormone** (prostaglandin E1)-induced AMP formation. [3H]Arachidonate and the three [3H]monoHETEs all rapidly labeled the membrane lipids of intact N1E-115 cells, with each [3H]eicosanoid **producing** a unique labeling profile. [3H]15-HETE labeling was noteworthy in that 85% of the label found in the phospholipids was in phosphatidylinositol (PI) (half-time to steady state = 3 min). Exogenous 15-HETE inhibited the labeling of PI by [3H]arachidonate (IC50 = 28 μM) and elevated unesterified [3H]arachidonate levels. Thus, the mechanism of blockade of receptor-mediated cGMP responses by monoHETEs is likely to be more complex than the simple inhibition of cytosolic mechanisms, e.g., generation of a putative 2nd messenger by lipoxygenase, and may involve also alterations of membrane function accompanying the redistribution of esterified arachidonate.

L19 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:471436 HCAPLUS

DOCUMENT NUMBER: 107:71436
TITLE: The action of peptides and proteases on the arachidonate cascade of human and rat platelets
AUTHOR(S): Gecse, A.; Mezei, Zs.; Telegdy, G.
CORPORATE SOURCE: Med. Sch., Univ. Szeged, Szeged, 6701, Hung.
SOURCE: Advances in Experimental Medicine and Biology (**1986**), 198B(Kinins 4, Pt. B), 121-8
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The arachidonate cascades of human or rat platelets were modified by peptides (bradykinin, angiotensin I, angiotensin II, Asp1-Val5-angiotensin II-amide, somatostatin) and proteases (trypsin, kallikrein). The lipoxygenase pathway was not altered by angiotensin I, angiotensin II, trypsin, or kallikrein, whereas the synthesis some of the cyclooxygenase **products** was selectively changed by these substances. Bradykinin and somatostatin resulted in an attenuated formation of 12-hydroperoxy-5,8,10,14-eicosatetraenoic acid and 12-hydroxy-5,8,10-heptadecatrienoic acid (U-shaped, dose-response curve) and at the same time the synthesis of cyclooxygenase metabolites was increased (bell-shaped, dose-response curve). Asp1-Val5-angiotensin II-amide increased the synthesis of lipoxygenase **products** and diminished the formation of TXB2. At the same time this peptide selectively induced the enzymic release of PGD2 from platelets. These peptides and proteolytic enzymes might have physiol. significance in the balance between lipoxygenase and cyclooxygenase metabolites and in the release of proaggregatory and antiaggregatory substances from platelets.

L19 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:28027 HCAPLUS
DOCUMENT NUMBER: 106:28027
TITLE: Transmembrane signals mediating neural peptide secretion: role of protein kinase C activators and arachidonic acid metabolites in luteinizing **hormone**-releasing **hormone** secretion
AUTHOR(S): Negro-Vilar, Andres; Conte, Domenico; Valenca, Marcelo
CORPORATE SOURCE: Lab. Reprod. Dev. Toxicol., Natl. Inst. Environm. Health Sci., Research Triangle Park, NC, 27709, USA
SOURCE: Endocrinology (**1986**), 119(6), 2796-802
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of different activators of protein kinase C on the secretion of LH-RH [9034-40-6] from rat median eminence nerve terminals incubated in vitro were examined The release of PGE2 [363-24-6], a metabolite of arachidonic acid [506-32-1] intimately involved in the secretion of LH-RH, was also evaluated. Synthetic diacylglycerol [1,2-didecanoylglycerol (DiC10) [17863-69-3]] significantly enhanced PGE2 release in a concentration-dependent manner. Blockade of phospholipase A2 (PLA2) [9001-84-7] activity nullified this effect. LH-RH release, on the other hand, was not increased by DiC10. However, in the presence of a lipoxygenase [9029-60-1] inhibitor, DiC10 **produced** a concentration-related increase in LH-RH release, which paralleled that in PGE2. Phospholipase C (PLC) [9001-86-9] increased both PGE2 and LH-RH secretion. Again, blockade of the lipoxygenase pathway enhanced the release of LH-RH by PLC without affecting the stimulated secretion of PGE2. A phorbol ester, phorbol 12,13-dibutyrate (PDBu) [37558-16-0], markedly increased LH-RH secretion but induced a modest increase in PGE2 release. Both effects of PDBu were unaffected by lipoxygenase inhibition.

DiC10, PDBu, and PLC significantly augmented LH-RH secretion from tissues in which metabolism of arachidonic acid was prevented by inhibition of both cyclooxygenase and lipoxygenase pathways, suggesting that activation of protein kinase C, independent of PLA2 activation, leads to the secretion of this neuralpeptide. Some lipoxygenase metabolites had either no effect on [5- [71030-39-2] and 15-hydroxyeicosatetraenoic (15-HETE) [71030-36-9]] or induced a marginal stimulation of (**12-HETE** [**71030-37-0**]) LH-RH release. At certain concns., **12-HETE** enhanced the stimulatory effect of the phorbol ester on LH-RH release. Evidently, activation of protein kinase C stimulates LH-RH secretion from nerve terminals in vitro and, further, diacylglycerol may represent an important intracellular messenger participating in the events leading to LH-RH secretion. In addition, stimulation with DiC10 and PLC uncovered inhibitory [unknown arachidonic acid metabolite(s) via lipoxygenase] and stimulatory (PGE2 via cyclooxygenase [39391-18-9]) pathways through with arachidonic acid metabolites may participate in the intracellular transduction of signals modulating neural peptide secretion.

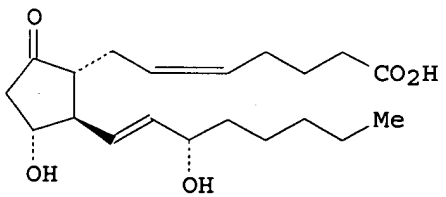
L19 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:570483 HCAPLUS
DOCUMENT NUMBER: 105:170483
TITLE: Opposite effects of adrenalectomy on eicosanoid release in rat peritoneal macrophages and spleen
AUTHOR(S): Vincent, J. E.; Zijlstra, F. J.; Van Der Broek, A. M. W. C.; Gezel, T. E.
CORPORATE SOURCE: Fac. Med., Erasmus Univ. Rotterdam, Rotterdam, 3000 DR, Neth.
SOURCE: Prostaglandins (**1986**), 32(1), 132-6
CODEN: PRGLBA; ISSN: 0090-6980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of adrenalectomy on the formation of cyclooxygenase and lipoxygenase **products** by activated peritoneal rat macrophages was determined and compared with that of the spleen. After isolation, the cells and tissues were incubated with [1-14C]arachidonic acid and the Ca-ionophore A23187 and the metabolites were isolated by HPLC. The main components formed in the macrophages of the controls are 6-keto-PGF1α, TxB2 and 12-hydroxyeicosatetraenoic acid ( **12-HETE**). One peak represents 5,12-dihydroxy HETE. Smaller amts. of PGF2α, PGE2, PGD2, LTB4 and 15-HETE are also present. After adrenalectomy, a considerable increase occurs in the amts. of LTB4, 15-HETE and **12-HETE.** The increase in the prostaglandins is smaller. The compds. formed from endogenous arachidonic acid were determined In the cells of the controls, the formation of LTB4 is considerably increased after adrenalectomy. In the spleen, PGD2 and **12-HETE** are decreased after adrenalectomy. The effect in the macrophages is most probably related to a diminished amount or inactivation of lipocortin, a glucocorticosteroid-induced peptide with phospholipase A2 inhibitory activity in adrenalectomized animals. In the decrease in formation in the spleen, the absence of the permissive effect of glucocorticosteroids on the **hormone**-induced lipolysis may play a role.

L19 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:21633 HCAPLUS
DOCUMENT NUMBER: 102:21633
TITLE: Arachidonic acid, 12- and 15-hydroxyeicosatetraenoic acids, eicosapentaenoic acid, and phospholipase A2 induce starfish oocyte maturation

AUTHOR(S): Meijer, Laurent; Guerrier, Pierre; Maclouf, Jacques
CORPORATE SOURCE: Stn. Biol. Roscoff, Roscoff, 29211, Fr.
SOURCE: Developmental Biology (Orlando, FL, United States) (**1984**), 106(2), 368-78
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In starfish, oocyte maturation (meiosis reinitiation) is induced by 1-methyladenine (I). Arachidonic acid (AA) induces oocyte maturation at concns. of >0.5 μM. This maturation shares many characteristics with I-induced maturation: same kinetics, same required contact time, same stimulation of protein phosphorylation and Na+ influx. Although Ca2+ facilitates the AA-induced, but not the I-induced maturation, AA, like I, does not stimulate Ca2+ uptake. Ca2+ does not facilitate AA uptake by oocytes. Out of 36 different fatty acids (saturated and unsatd.), only AA and eicosapentaenoic acids were found to mimic I. Ca2+-dependent phospholipases A2 from bee venom and Naja venom also induce maturation (0.1-1 unit/mL) when added externally to the oocytes. Phospholipase A2 inhibitors (quinacrine, bromophenacyl bromide) block maturation; inhibition is reversed by increasing the I concentration and only occurs during the **hormone**-dependent period. AA is usually metabolized through oxidation by cyclooxygenase or lipoxygenase. Cyclooxygenase inhibitors (acetylsalicylic acid, indomethacin, tolazoline) do not block maturation; prostaglandins E2, D2, F2α, I2 and thromboxane B2 do not induce meiosis reinitiation. On the other hand, lipoxygenase inhibitors (quercetin, BHT, and eicosatetraynoic acid) block I-induced maturation; although leukotrienes (A4, B4, C4, D4, E4) have no effects on oocytes, 2 other lipoxygenase **products**, 12- and 15-hydroxyeicosatetraenoic acids (and their corresponding hydroperoxy acids) induce oocyte maturation (.apprx.1 μM). The possible mode of action of the fatty acids inducing oocyte maturation is discussed.

L19 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:12083 HCAPLUS
DOCUMENT NUMBER: 98:12083
TITLE: The use of glomerular cell culture to evaluate cyclo-oxygenase and lipoxygenase **products** of arachidonic acid metabolism in the kidney
AUTHOR(S): Dunn, Michael J.; Petrulis, Alice S.; Scharschmidt, Linda S.; Jim, Kam; Hassid, Aviv
CORPORATE SOURCE: Univ. Hosp. Cleveland, Case West. Reserve Univ., Cleveland, OH, 44106, USA
SOURCE: INSERM Symposium (**1982**), 21(Biochem. Kidney Funct.), 3-12
CODEN: INSSDM; ISSN: 0378-0546
DOCUMENT TYPE: Journal
LANGUAGE: English
GI




I

AB cyclooxygenase [39391-18-9] And lipoxygenase [9029-60-1] **products** were evaluated in isolated rat kidney glomerular mesangial and epithelial cells in culture. In epithelial cells, PGE2 (I) [363-24-6] was the most abundant cycloxygenase **product** found followed by TXB2 [54397-85-2]. Cyclooxygenase **product** formation was stimulated by arachidonate [506-32-1] or the Ca ionophore, A 23187. I formation was specifically stimulated by angiotensin peptides. Evidently, receptor occupancy on the cell membrane by angiotensin II [11128-99-7] releases arachidonate by a lipoxygenase to a pool of cyclooxygenase linked specifically to I formation. hydroxyeicosatetraenoic acid [**71030-37-0**] Was the main lipoxygenase **product** in epithelial cultures. Mesangial cells **synthesized** large amts. of I and smaller amts. of PGF2α [551-11-1] and 6-keto-PGF1α [58962-34-8]. arginine vasopressin (AVP) [113-79-1] stimulated I formation by mesangial cells as did angiotensin II. An antipressor analog of AVP blocked I formation by AVP. Antidiuretic nonpressor analogs of AVP had no such effect. AVP-induced formation of I by mesangial cells apparently affects mesangial contraction and consequently glomerular filtration. Verapamil decreased vasopressin-stimulated I formation, indicating involvement of Ca. Similarities between I stimulation by AVP in mesangial cells and by angiotensin II in epithelial cells are discussed.

L19 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:183961 HCAPLUS
DOCUMENT NUMBER: 90:183961
TITLE: Prostaglandin **production** by type II alveolar epithelial cells
AUTHOR(S): Taylor, Linda; Polgar, Peter; McAteer, James; Douglas, William H. J.
CORPORATE SOURCE: Sch. Med., Boston Univ., Boston, MA, USA
SOURCE: Biochimica et Biophysica Acta (**1979**), 572(3), 502-9
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostaglandin **production** was studied in fetal and adult type II alveolar epithelial cells. Two culture systems were employed, fetal rat lung organotypic cultures consisting of fetal type II cells and monolayer cultures of adult lung type II cells. Dexamethasone, thyroxine, prolactin, and insulin, **hormones** which influence lung development, each reduced the **production** of PG E and Fα by the organotypic cultures. The fetal cultures **produced** relatively large quantities of PG E and Fα and smaller quantities of 6-oxoPG F1α and thromboxane B2. However, PG E2 **production** was predominant. In contrast, the adult type II cells in monolayer culture **produced** predominantly prostacyclin (6-oxoPG F1α) along with smaller quantities of PG E2 and PG F2α. The type II cells were relatively unresponsive to prostaglandins. Exogenously added PG E2 had no effect on cell growth, and only a minimal effect on cyclic AMP levels in the monolayer cultures.

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=> d que stat l18
L1             3 SEA FILE=REGISTRY ABB=ON  (12-HETE OR 11,12-EET)/CN
L2             1 SEA FILE=REGISTRY ABB=ON  "EPOXYEICOSATRIENOIC ACID"/CN
L3             4 SEA FILE=REGISTRY ABB=ON  L1 OR L2
L4             1 SEA FILE=REGISTRY ABB=ON  "12-HYDROPEROXY-5,8,10,14-EICOSATETRA
                 ENOIC ACID"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  "13-HYDROPEROXY-9Z,11E,15Z-OCTADECATR
                 IENOIC ACID"/CN
L6             1 SEA FILE=REGISTRY ABB=ON  "13-HYDROPEROXY-9-CIS-11-TRANS-OCTADE
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L9          1467 SEA FILE=HCAPLUS ABB=ON  (L3 OR 12-HETE OR 11,12-EET) AND
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L10          857 SEA FILE=HCAPLUS ABB=ON  (?CHONDRUS? OR RED?(W)?ALGAE?) AND
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                 ?ACROCHAETE?(W)?OPERCULATA? OR L7 OR 12-HPETE OR 13-HPOTE OR
                 13-HPODE)
L11            2 SEA FILE=HCAPLUS ABB=ON  L9 AND L10
L12           33 SEA FILE=HCAPLUS ABB=ON  L9 AND (?THALLUS? OR ?HORMONE?)
L13           34 SEA FILE=HCAPLUS ABB=ON  L11 OR L12
L14            1 SEA FILE=REGISTRY ABB=ON  NITROGEN/CN
L16           71 SEA L13
L17           55 DUP REMOV L16 (16 DUPLICATES REMOVED)
L18            4 SEA L17 AND (L14 OR ?NITROGEN? OR HOT? OR ?HEAT? OR ?COLD?)

=> d ibib abs l18 1-4

L18  ANSWER 1 OF 4  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
ACCESSION NUMBER:   2003409284  EMBASE
TITLE:              Reviews: Current topics role of nuclear receptors in the
                    regulation of gene expression by dietary fatty acids
                    (review).
AUTHOR:             Khan S.A.; Vanden Heuvel J.P.
CORPORATE SOURCE:   J.P. Vanden Heuvel, Department of Veterinary Science, Ctr.
                    Molec. Toxicol./Carcinogenesis, Penn State University,
                    University Park, PA 16802, United States. jpv2@psu.edu
SOURCE:             Journal of Nutritional Biochemistry, (1 Oct 2003) 14/10
                    (554-567).
                    Refs: 142
                    ISSN: 0955-2863  CODEN: JNBIEL
COUNTRY:            United States
DOCUMENT TYPE:      Journal; General Review
FILE SEGMENT:       030     Pharmacology
                    037     Drug Literature Index
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   Long chain fatty acids, derived either from endogenous metabolism or by
     nutritional sources play significant roles in important biological
     processes of membrane structure, production of biologically
     active compounds, and participation in cellular signaling processes.
     Recently, the structure of dietary fatty acids has become an important
     issue in human health because ingestion of saturated fats (containing
     triglycerides composed of saturated fatty acids) is considered harmful,
     while unsaturated fats are viewed as beneficial. It is important to note
     that the molecular reason for this dichotomy still remains elusive. Since
     fatty acids are important players in development of pathology of
     cardiovascular and endocrine system, understanding the key molecular
     targets of fatty acids, in particular those that discriminate between
     saturated and unsaturated fats, is much needed. Recently, insights have
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been gained on several fatty acid-activated nuclear receptors involved in gene expression. In other words, we can now envision long chain fatty acids as regulators of signal transduction processes and gene regulation, which in turn will dictate their roles in health and disease. In this review, we will discuss fatty acid-mediated regulation of nuclear receptors. We will focus on peroxisome proliferators-activated receptors (PPARs), liver X receptors (LXR), retinoid X receptors (RXRs), and Hepatocyte Nuclear Factor alpha (HNF-4α), all of which play pivotal roles in dietary fatty acid-mediated effects. Also, the regulation of gene expression by Conjugated Linoleic Acids (CLA), a family of dienoic fatty acids with a variety of beneficial effects, will be discussed. .COPYRGT. 2003 Elsevier Inc. All rights reserved.

L18 ANSWER 2 OF 4 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 950956948 JICST-EPlus
TITLE: Synthesis of 2(1H)-Quinolinone Derivatives and Their Inhibitory Activity on the Release of 12(S)-Hydroxyeicosatetraenoic Acid (**12-HETE**) from Platelets.
AUTHOR: UNO T; OZEKI Y; KOGA Y; CHU G-N; TAMURA K; IGAWA T; UNEMI F; KIDO M; NISHI T
CORPORATE SOURCE: Otsuka Pharmaceutical Co., Ltd., Tokushima, JPN
SOURCE: Chem Pharm Bull, (1995) vol. 43, no. 10, pp. 1724-1733. Journal Code: G0504A (Fig. 2, Tbl. 4, Ref. 26)
CODEN: CPBTAL; ISSN: 0009-2363
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
AB A search for potent inhibitors of release of 12(S)-hydroxyeicosatetraenoic acid (**12-HETE**), which plays an important role in the pathogenesis of various circulatory disorders and arteriosclerosis, led us to 6-¢4-(1-cyclohexyl-5-tetrazolyl)butoxy!-3,4-dihydro-2(1H)-quinolinone (cilostazol) and 2(1H)-quinolinone derivatives having an azole group in the side chain. Many 2(1H)-quinolinone derivatives were **synthesized** and tested in vitro for the inhibitory activity in human platelets. 3,4-Dihydro-6-¢3-(1-o-tolylimidazol-2-yl)sulfinylpropoxy!-2(1H)-quinolinone (5k) was found to be one of the most potent inhibitors of **12-HETE** release, being more potent than esculetin. In addition, the sulfoxide 5k showed in vivo inhibitory activity on platelet adhesion in rats. Since 5k is racemic, the enantiomers were **prepared** and their potencies were compared in vitro and in vivo. (S)-(+)-5k had the best pharmacological profile and was selected as a candidate drug for further development. The structure-activity relationships are discussed. (author abst.)

L18 ANSWER 3 OF 4 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 900589844 JICST-EPlus
TITLE: Melanocyte-stimulating properties of proinflammatory chemical mediators.
AUTHOR: MAEDA KAZUHISA; TOMITA YASUSHI; TAGAMI HACHIRO
CORPORATE SOURCE: Tohoku Univ., School of Medicine
SOURCE: Ensho (Japanese Journal of Inflammation), (1990) vol. 10, no. 3, pp. 189-194. Journal Code: Y0899A (Fig. 3, Tbl. 2, Ref. 20)
CODEN: ENSHEE; ISSN: 0389-4290
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB Skin darkening after cutaneous inflammation is a well known phenomenon but its mechanisms for this hyperpigmentation have not been clarified yet. Because in inflamed skin various mediators such as arachidonic acid metabolites and histamine are found in increased amounts, we have studied their effects on cultured normal human melanocytes. As reported previously we have found that prostaglandine E2 stimulated normal human melanocytes. In addition histamine, platelet activating factor, bradykinin and arachidonic acid metabolites such as leukotriene(LT) C4 and LTD4 also stimulated melanocytes. They were found to increase the total amounts of immunoreactive tyrosinase and tyrosinase related protei, the number of dendrites and the size of melanocytes. In these proinflammatory mediators, LTC4 and histamine showed far strong stimulatory effect. On the other hand, serotonin, heparin and other arachidonic acid metabolites such as PGE1 PGFs and 12-hydroxy eicosatetraenoic acid(**12-HETE** ) did not show any significant stimulatory effect. Present studies suggest that various proinflammatory chemical mediators, especially LTC4 and histamine are involved in the stimulation of melanocytes to accelerate the **production** of melanine and its active transfer to neighboring keratinocytes, resulting into the formation of hyperpigmentation after skin inflammation. (author abst.)

L18 ANSWER 4 OF 4 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 860311979 JICST-EPlus
TITLE: Effects of flavonoids and related compounds from mulberry tree on arachidonate metabolism in rat platelet homogenates.
AUTHOR: KIMURA Y; OKUDA H
NOMURA T; FUKAI T
ARICHI S
CORPORATE SOURCE: Ehime Univ.
Toho Univ., Funabashi
Kinki Univ., Osaka
SOURCE: Chem Pharm Bull, (1986) vol. 34, no. 3, pp. 1223-1227.
Journal Code: G0504A (Fig. 2, Ref. 10)
CODEN: CPBTAL; ISSN: 0009-2363
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New

AB The effects of various flavonoids and related compounds isolated from the root bark of mulberry tree on rat platelet lipoxygenase and cyclooxygenase **products** formed from ¢1-14C! arachidonic acid were studied. Morusin was found to inhibit the formations of 12-hydroxy-5,8,10-heptadecatrienoic acid (HHT) and thromboxane B2 (cyclooxygenase **products**) more strongly than the formation of 12-hydroxy-5,8,10,14-eicosatetraenoic acid (**12-HETE**) (12-lipoxygenase **product**). Oxydihydromorusin and kuwanon C were also found to inhibit the formation of thromboxane B2 more strongly than the formations of HHT and **12-HETE.** Mulberrofuran A inhibited the formations of HHT and thromboxane B2, but it increased the formation of **12-HETE.** Albanol B and mulberrofuran F did not affect arachidonate metabolism in rat platelet homogenates. (author abst.)

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=> d his ful

     FILE 'REGISTRY' ENTERED AT 13:49:39 ON 09 MAR 2005
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                 E 11,12-EET/CN
                 E EPOXYEICOSATRIENOIC ACID/CN
L2             1 SEA ABB=ON  "EPOXYEICOSATRIENOIC ACID"/CN
                 D
L3             4 SEA ABB=ON  L1 OR L2
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L4             1 SEA ABB=ON  "12-HYDROPEROXY-5,8,10,14-EICOSATETRAENOIC
                 ACID"/CN
                 E 13-HYDROPEROXY-9,11-/CN
L5             1 SEA ABB=ON  "13-HYDROPEROXY-9Z,11E,15Z-OCTADECATRIENOIC
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L6             1 SEA ABB=ON  "13-HYDROPEROXY-9-CIS-11-TRANS-OCTADECADIENOIC
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L7             3 SEA ABB=ON  L4 OR L5 OR L6
L8             3 SEA ABB=ON  (ARACHIDONIC ACID OR LINOLENIC ACID OR LINOLEIC
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L10          857 SEA ABB=ON  (?CHONDRUS? OR RED?(W)?ALGAE?) AND (?PEPTID? OR
                 ?LIPID? OR ?SACCHARID? OR ?GREEN?(W)?ALGAE? OR ?ACROCHAETE?(W)?
                 OPERCULATA? OR L7 OR 12-HPETE OR 13-HPOTE OR 13-HPODE)
L11            2 SEA ABB=ON  L9 AND L10
L12           33 SEA ABB=ON  L9 AND (?THALLUS? OR ?HORMONE?)
L13           34 SEA ABB=ON  L11 OR L12  34 cits from CA Plus

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     FILE 'HCAPLUS' ENTERED AT 14:03:47 ON 09 MAR 2005
L15            0 SEA ABB=ON  L13 AND (L14 OR ?NITROGEN? OR HOT? OR ?HEAT? OR
                 ?COLD?)

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 14:04:54 ON
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L16           71 SEA ABB=ON  L13
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L18            4 SEA ABB=ON  L17 AND (L14 OR ?NITROGEN? OR HOT? OR ?HEAT? OR
                 ?COLD?)  4 cits from other database

     FILE 'HCAPLUS' ENTERED AT 14:07:11 ON 09 MAR 2005
L19           30 SEA ABB=ON  L13 AND (PRD<20020802 OR PD<20020802)
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Precision in these results is lacking. When I found so few that matched all your requirements, I did a broader search.

MJR